

REMARKS

Claims 1 and 71 to 79 are pending in this patent application. Claims 1 and 76 have been amended herein to recite more conventional claim language, and the amendments do not introduce new matter into the application. No new claims have been added, and no claims have been canceled, herein.

Applicants acknowledge with appreciation the time and courtesies extended by the Examiner toward applicants' representative during the telephonic interview of January 9, 2009. As was discussed during the interview, applicants respectfully submit that the pending claims are not rendered obvious by Yu in view of the Stec and Summerton patents, for at least the reasons set forth below.

Applicants respectfully request reconsideration of the rejections of record in view of the foregoing amendments and the following remarks.

Alleged Double Patenting

Claims 1 and 71 to 79 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1, 5, 8, 19 to 22, 54, 57, and 63 of copending U.S. patent application number 10/700,697. Claims 1 and 71 to 79 have also been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1, 7 to 9, 16, 18 to 22, 26 to 31, 73, and 76 to 85 of copending U.S. patent application number 10/701,264. Finally, claims 1 and 71 to 79 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1, 5, 9, 11, 75, 78, and 93 to 97 of copending U.S. patent application number 10/701,316.

Without acquiescing that there has been an adequate showing that those of ordinary skill in the art would have found the cited claims to have been obvious in view of the claims of the referenced patent applications, applicants nonetheless submit herewith the requested terminal disclaimers. This is being done solely in an attempt to advance prosecution of the present patent application, and should not be construed to constitute an acknowledgment of obviousness or any other substantive relationship among the involved patent claims.

Alleged Obviousness

Claims 1 and 71 and 79 have been rejected under 35 U.S.C. § 103(a) as allegedly rendered obvious by Yu, Y., *et al.*, *RNA*, 1997, 3, 324-331 (“the Yu article”) in view of U.S. patent number 5,151,510 (“the Stec patent”) and U.S. patent number 5,142,047 (“the Summerton patent”). Applicants respectfully request reconsideration and withdrawal of this rejection because the claimed compounds would not have been obvious to those of ordinary skill in the art before applicants’ invention.

To establish *prima facie* obviousness, the Patent Office must demonstrate that the cited prior art reference or combination of references teaches or suggests all the limitations of the claims.¹ The Patent Office must also identify “a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.”² In other words, the Office must identify “an apparent reason to combine the known elements *in the fashion claimed by the patent at issue*. To facilitate review, this analysis should be made explicit.”³

Claim 1 recites a compound comprising first and second chemically synthesized oligomeric compounds, wherein the first chemically synthesized oligomeric compound is complementary to the second chemically synthesized oligomeric compound and to a selected target mRNA, and wherein each of the first and said second chemically synthesized oligomeric compounds comprises at least one modified nucleoside comprising a sugar surrogate.

The cited references fail to provide any reason that would have led those skilled in the art to produce the claimed compounds before applicants’ invention. For example, the Yu article describes a method of identifying methylated nucleosides in natural ribosomal RNA molecules (rRNA).⁴ As described in the article, some ribonucleosides in eukaryotic rRNA are modified by methylation at the 2’ position of sugar groups.⁵ The Yu article describes an assay for identifying whether a particular nucleoside comprises such a methylated sugar. The assay described in the

¹ *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974); *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970).

² *KSR Int’l Co. v. Teleflex*, 127 S.Ct. 1727, 1741.

³ *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (emphasis added)(citing *In re Kahn*, 441, F.3d 977, 988 (Fed. Cir. 2006).

⁴ The Yu article, abstract.

⁵ *Id.* at page 324.

article involves hybridization of the native rRNA with a DNA-containing oligonucleotide, followed by exposure to RNase H. Since RNase H cleaves the non-methylated RNA strand of an RNA/DNA duplex, but does not cleave methylated RNA, the assay can be used to determine whether the original rRNA was methylated by detection of cleavage.⁶ Significantly, the Yu article fails to describe or suggest the claimed compounds, however.

The Office combines the Yu article with the Stec and Sumerton patents, which describe certain modifications that can be incorporated into RNA, to support the assertion that the present invention “as a whole” would have been obvious.⁷ The Office fails to provide, however, any reason why (1) one would apply the assay described in the Yu article to mRNA, (2) one would perform the assay on chemically synthesized oligomeric compounds comprising modifications, and (3) one would include the particular modifications claimed in either strand of an RNA duplex. For at least these reasons, the Yu article in view of the Stec and Summerton patents would not have rendered the claimed compounds obvious.

Those skilled in the art would not have utilized mRNA as a substrate in the assay described in the Yu article, rather than rRNA, as the Office asserts. The purpose of the assay described in the article is to characterize *natural rRNA*. Since natural rRNA is methylated at certain positions, it is useful to have an assay to identify which positions are methylated and which ones are not. The Office remarks that one skilled in the art would substitute mRNA for rRNA in the assay described in the Yu article “in order to determine if any sites within the mRNA are methylated.” Applicants are unaware of any evidence, and the Office has not provided any evidence, demonstrating that natural mRNA contains nucleosides having 2'-methyl modifications. Accordingly, there would have been no reason to utilize the assay described in the Yu article for mRNA. Accordingly, the article provides no reason that would have prompted one skilled in the art to produce a compound comprising first and second oligomeric compounds wherein the first oligomeric compound is complementary to the second oligomeric compound and to an mRNA, as claimed.

Even if one skilled in the art would have used the assay described in the Yu article to characterize mRNA, despite having had no reason to do so, there still would have been no reason

⁶ *Id.* at page 325 and at Figure 1.

⁷ Office action dated July 10, 2008, page 6.

to perform the assay on a synthetic oligomeric compound comprising chemical modifications. The purpose of the assay described in the Yu article is to characterize naturally occurring RNA. That purpose would have been defeated by replacing natural RNA, the object of the assay, with a synthetic oligonucleotide comprising chemical modifications, as claimed. The Yu article thus would have provided no reason to produce a compound comprising first and second chemically synthesized oligomeric compounds wherein each oligomeric compound comprises chemical modifications, as claimed.

Finally, even if one skilled in the art would have performed the assay described in the Yu article using mRNA, despite having had no reason to do so, and even if one would have used a synthetic mRNA comprising chemical modifications in the assay, despite having defeated the purpose of the assay in doing so, one still would have had no reason to select the particular chemical modifications recited in the claims: sugar surrogates, including, but not limited to, pyrrolidine nucleosides, morpholino nucleosides, cyclobutyl nucleosides and peptide nucleic acid nucleosides; and phosphorothioate linkages. The Office provides no reason why one of skill would have introduced these *particular* chemical modifications, as opposed to other types of modifications, in either strand of the duplex described in the Yu article, but cites the Stec and Summerton patents for alleged description of chemical modifications amenable to RNA molecules that are not described in the Yu article. The Stec and Summerton patents fail to provide any reason that would have led one skilled in the art to modify the duplex described in the Yu article, however, and thus fail to remedy the deficiencies of the article.

For at least the reasons discussed above, the claimed compounds would therefore not have been rendered obvious by the Yu article in view of the Stec and Summerton patents. Applicants accordingly, respectfully, request withdrawal of the rejection.

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Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the official action of record. Accordingly, an early and favorable action is respectfully requested.

Respectfully submitted,

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